

Alternatively activated dendritic cells derived from systemic lupus erythematosus patients have tolerogenic phenotype and function

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Background: Tolerogenic dendritic cells (DCs) are potential cell-based therapy in autoimmune diseases.

Methods: In this study, we generated alternatively activated DCs (aaDCs) by treating monocyte-derived DCs from patients with systemic lupus erythematosus (SLE) and healthy subjects with combination of 1,25 dihydroxyvitamin D(3) (vitD3) and dexamethasone followed by lipopolysaccharide-induced maturation.

Results: Lupus aaDCs were found to acquire semi-mature phenotype that remained maturation-resistant to immunostimulants. They produced low level of interleukin-12 (IL-12) but high level of IL-10. They had attenuated allostimulatory effects on T cell activation and proliferation comparable to normal aaDCs and demonstrated differential immunomodulatory effects on naïve and memory T cells. These aaDCs were capable of inducing IL-10 producing regulatory T effectors from naïve T cells whereas they modulated cytokine profile with suppressed production of interferon- γ and IL-17 by co-cultured memory T cells with attenuated proliferation.

Conclusions: These aaDCs were shown to be superior than those generated using vitD3 alone in lupus patients.

Efficacy and tolerability of long-term tacrolimus treatment in lupus nephritis

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Introduction: Tacrolimus (TAC) is an emerging treatment for lupus nephritis (LN), but long-term data of this therapy are lacking.

Methods: We retrospectively reviewed 27 LN patients who received TAC treatment for 46.9 \pm 37.9 months.

Results: In 17 patients with class III/IV or V LN and persistent proteinuria of >2 g/day despite induction immunosuppression, add-on TAC treatment resulted in response rates of 66.7% and 80.0%, respectively. In 10 patients with nephrotic syndrome due to class V LN, prednisolone and TAC as initial treatment was associated with response rates of 60.0% and 90.0% after 12 and 24 months, respectively. The overall proteinuria dropped from 3.6 \pm 2.6 g/d to 1.0 \pm 1.1 g/d (P <0.05). Four patients developed end-stage kidney disease, with 3-, 5-, and 8-year renal survival rates of 93%, 83%, and 83%, respectively. In the remaining patients, serum creatinine and estimated glomerular filtration rate remained stable after 36 months. One patient with pre-existing chronic renal failure developed TAC nephrotoxicity. Four renal relapsed occurred, and all were associated with low TAC blood levels. Six (20.1%) patients had deterioration of hypertension and one (3.4%) patient had new-onset diabetes mellitus. Six (20.1%) patients had infections that required hospitalisation. Two patients succumbed, and was due to pneumonia and breast cancer respectively.

Conclusion: The results suggest efficacy of TAC in LN, especially in reducing proteinuria. Its role as long-term maintenance agent remains to be examined.